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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

IN RE: ROTHSCHILD et al.	**APPEAL NO. _____**
SERIAL NO: 09/900,063	
FOR: PROLACTIN RECEPTOR GENE AS A GENETIC MARKER FOR INCREASED LITTER SIZE IN ANIMALS	**BRIEF ON APPEAL**
FILED: July 6, 2001	
GROUP ART UNIT: 1634	

To the Commissioner of Patents and Trademarks

Mail Code APPEAL BRIEF
P. O. Box 1450
Alexandria, VA 22313-1450

Dear Sirs:

Appellants respectfully request that the following Reply Brief be entered into the record. It addresses new arguments set forth in the Examiner's Answer.

CERTIFICATE OF MAILING BY EXPRESS MAIL

I hereby certify that this document and the documents referred to as enclosed therein are being deposited with the U. S. Postal Service in an envelope as "Express Mail Post Office to Addressee" addressed to: Commissioner of Patents, P. O. Box 1450, Alexandria, VA 22313-1450, prior to 5:00 p.m. on 30th day of June, 2004.

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I. Introduction

The Examiner's written description rejection relate primarily to the issues of whether, (1) Appellants' have or must show a number of polymorphisms which are representative of the genus of any polymorphisms associated with litter size, (2) whether there is no structure function relationship between undisclosed polymorphisms in the prolactin receptor sequence and litter size, and (3) whether there is structure or function present for any species other than pig. Based on these interpretations of Appellants' claimed invention, the Examiner argues that there is insufficient descriptive support for the current claims. As shown below, however, the Examiner's rejections are based on incorrect interpretations of Appellant's invention.

The Examiner also maintains the rejection based on lack of enablement due to perceived undue experimentation, breadth of the claims, and unpredictability. Based on these findings by the Examiner, it is argued that the specification does not enable one skilled in the art to practice the invention. As further shown below, however, the Examiner's rejections are based on an improper application of enablement law to Appellants' claimed invention. For these reasons, the Examiner's rejections should be summarily reversed.

II. The Examiner's Conclusion that Appellants have Inadequately Described the Invention by not Providing a Representative Number of Species is Based on an Inadequate Application of the Law to Appellant's Invention

The Examiner incorrectly states that the genus of polymorphisms encompassed by Appellant's claims represents every possible variation which could occur in SEQ ID NO: 3.

(Examiner's Answer, p. 10). The Examiner then notes that the Federal Circuit in *Eli Lilly* stated "[a] description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." *Regents of University of California v. Eli Lilly*, 119 F.3d 1559, 1569 (Fed. Cir. 1997) (Examiner's Brief, p. 11). The Examiner finally notes that Appellant's disclosed species are not representative of the genus of polymorphisms as a whole. (Examiner's Brief, p. 11).

Appellants demonstrated in their Brief on Appeal that the Examiner's interpretation of Appellant's claimed invention was erroneous since the Examiner has failed to understand that Appellants' invention relates to the association of the region of the prolactin receptor gene as set forth in SEQ ID NO: 3 to the phenotypic trait of increased litter size. Thus, each species within the genus encompassed by Appellant's claims all share the common attribute of being quantitative trait loci that have a measurable effect on litter size that are all within SEQ ID NO: 3.

The Examiner states that Appellants have correctly set forth the legal framework underlying the written description guidelines. (Examiner's Answer, p. 10). As stated in Brief on Appeal, the Federal Circuit has stated that a genus claim may be adequately described where there is a "recitation of structural features common to the members of the genus." *Regents of University of California*, 119 F.3d at 1569. Moreover, the USPTO's Written Description Guidelines states that a sufficient variety of species has been described to reflect

variation within the genus where "one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the member of the genus in view of the species disclosed."

Applying this correct legal standard to Appellants' invention, the Examiner argues that Appellants have not adequately demonstrated a representative number of species. However, Appellants have demonstrated that the structural feature common to all members of the genus is the prolactin receptor gene as set forth in, or a region therein, of SEQ ID NO: 3. Further, in order to fall within the scope of Appellant's invention, the variant screened for within the prolactin receptor gene, or a region therein, as set forth in SEQ ID NO: 3, must have the function of being associated with a phenotypic increase in litter size.

Identification of the relevant polymorphism is the means by which one practices the invention, i.e., the association between the prolactin receptor gene and increased litter size. Appellants have disclosed at least three polymorphisms that have been identified which correlate with a phenotypic difference in litter size. These polymorphisms are identified in the Application using the restriction enzymes AluI, HinFI, and Hpych21V. See specification, Examples 6 and 7, pages 35-51. The specification further demonstrates that different polymorphisms will have various associations with litter size and this may vary with different populations. See specification, Example 7, pages 38-54. Since one of skill in the art would recognize that Appellant's were in possession of the common attribute within the genus, i.e., the association between the prolactin receptor gene as set forth in SEQ ID NO: 3, or a region

thereof, and an increase in litter size, Appellant's have adequately described a representative number of species.

III. The Examiner Has Ignored the Structure Function Relationship Adequately Described by Appellants in their Specification

The Examiner raises the question of whether Appellants have disclosed a structure which is correlated with an increase in litter size. (Examiner's Answer, p. 11). The Examiner then states that the only structures given are two specific polymorphisms. (Examiner's Answer, p.11). Thus, according to the Examiner, there is no structure given which is correlated with an increase in litter size.

The Examiner's conclusion is improperly based on a misunderstanding of the invention claimed by Appellants. As noted above, Appellant's invention is properly characterized as the association of a region of the prolactin receptor gene as set forth in SEQ ID NO: 3 to the phenotypic trait of increased litter size. (Specification, p. 4). Appellants have discovered that the prolactin receptor gene is a major effect gene for litter size and are using polymorphisms as genetic markers in order to practice the invention. This discovery that a single gene in the pathway contributes a measurable effect on the phenotype of increased litter size is the focus of Applicant's invention. (Specification 2-4). As taught by the specification, once an association between a gene and a phenotypic trait (here, the prolactin receptor gene and increased litter size) has been identified it takes routine screening to find variability within that gene which will be useful as a marker for the phenotypic result. (Specification, p. 5).

The Examiner states that "[t]here is no structure in common between the specific nucleotide change at the AluI polymorphism and the Hpych21V polymorphism. More importantly, there is no structure in common between the specific change at either of the disclosed polymorphisms and any other polymorphism which may exist." (Examiner's Answer, p. 12). As noted above, Appellants are not claiming the polymorphism sequences as compositions of matter and therefore part of Appellants invention. Rather, the prolactin receptor gene, or region thereof, as set forth in SEQ ID NO: 3, is the structural element common to all species within Appellants' genus claim.

Polymorphisms are not the common structural element of Appellants' invention. Their identification is a means by which the invention, the association between the prolactin receptor gene as set forth in SEQ ID NO: 3 and increased litter size, can be practiced. Breeders can then ascertain the identity of animals which will have a tendency towards larger litters by screening the prolactin receptor gene, or a region thereof, as set forth in SEQ ID NO: 3 in order to determine if there is a variation within this gene.

By incorrectly arguing that Appellants' invention constitutes polymorphic nucleotide sequences as compositions of matter, the Examiner has mistakenly concluded that a structure-function relationship is not present within Appellants' invention. This conclusion should be ignored upon correctly classifying Appellants' invention as the correlation between the prolactin receptor gene as set forth in SEQ ID NO: 3 and an increase in litter size.

IV. The Examiner's Argument that the Claim Scope Broadly Encompasses All Animals is Misguided

The Examiner states that Appellants claims are not limited to pigs and therefore open to any animal in the world. The Examiner then concludes that because of this large genus, a representative number of species is not provided. (Examiner's Answer, p. 13-14).

Appellants' claims require that animal to be screened contain a prolactin receptor gene as set forth in SEQ ID NO: 3. The claims are thus not drawn to any animal in the world. The Examiner recognizes that prolactin is likely found only in mammals (which lactate). (Specification, p. 14). Furthermore, the specification teaches that the prolactin receptor gene is an essential gene for reproductive success in *mammals*. (Specification, p. 2-3).

The Examiner states that because the claims are drawn to screening for polymorphisms in any animal by using the prolactin receptor gene sequence of a pig, there is no structure function relationship present for any other animal other than pig. Appellants have shown above that the claim scope is limited to animals that contain the prolactin receptor gene, i.e. mammals. Further, the specification teaches that the prolactin receptor gene sequence is highly conserved and thus that other animals with prolactin receptor genes will contain the same quality of being able to use variants within the prolactin receptor gene as a marker for increased litter size. (Specification, p. 7). Evidence of this is found in Example 1 where Appellants used human and rabbit cDNA sequences encoding the prolactin receptor as degenerate primers to isolate and amplify pig DNA. (Specification, Example 1, p. 27-28). Appellants have demonstrated the similarities present in the prolactin receptor gene

present in mammals and thus that a structure function relationship is similarly present in mammals other than pig.

V. The Examiner's Argument that Appellants' Disclosure is Non-Enabling Incorrectly Applies the Law of Enablement to the Invention

The Examiner states that it is unpredictable whether a particular polymorphism is associated with litter size and that there is no evidence of other polymorphisms existing in other animals. The Examiner next states that the claim scope is overbroad because it encompasses every animal species. Finally, the Examiner states that an undue amount of experimentation is necessary to screen animals for a polymorphism.

As noted above, Appellants' invention does not encompass all animal species. It instead is limited to mammals (which contain the prolactin receptor gene). Because the prolactin receptor gene is highly conserved, as demonstrated by Example 1 in the specification, the linkage between the prolactin receptor gene of SEQ ID NO: 3 and an increase in litter size is enabled for all species containing the gene.

As Appellants noted in their brief on appeal, experimentation is permissible if it is routine and if guidance is provided directing such experimentation such that one skilled in the art would be able to practice an embodiment of the invention. *Ex Parte Forman*, 230 U.S.P.Q. 546, 547 (Bd. Pat. App. & Int'f 1986). The Examiner argues that it requires an undue amount of necessary experimentation in order to screen for the presence of other polymorphisms with the prolactin receptor gene. As Appellants stated in their brief on appeal, however, such experimentation is routine for one skilled in the art. An animals' DNA

is isolated and assayed for the presence of a polymorphism, techniques well known to one skilled in the art (specification, p. 10). Moreover, the specification provides a specific example of isolating and assaying for the presence of a polymorphism. (specification, Example 2, p. 28-29).

Whether or not a particular polymorphism is identified with an increase in litter size or whether there are additional polymorphisms which may be used as markers is taught by the specification. Appellants have shown that there is an association between the prolactin receptor gene and an increase in litter size. A breeder can screen an animal for variances within the prolactin receptor gene of SEQ ID NO: 3 and, if variation is present, correlate that variation with an increased litter size. This prevents the breeder from having to screen all other genes associated with the reproductive pathway.

Moreover, once variation within the prolactin receptor gene has been identified, one skilled in the art would be able to perform routine experimentation in order to associate that polymorphism with litter size. "Those skilled in the art can generate snps from this region, conduct association studies as illustrated here, so as to determine which marker or combination of markers can be used to select for those animals likely to have a higher breeding value for litter size." (specification, p. 51). A specific example of an association study is taught by the specification. See Example 7, pages 38-51. The Examiner's conclusion of lack of enablement is therefore misguided and should be ignored.

V. Conclusion

Therefore, for the above-stated reasons, and for the reasons set forth in Appellants' appeal brief, Appellants respectfully request reversal of the decision of the Examiner, and allowance of the application.

It is not believed a fee is due with this brief. If a fee is due, please consider this a request to debit or credit Deposit Account No. 26-0084 accordingly.

Respectfully submitted,

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